REMARKS

Claims 56 and 69 are pending in this application and were rejected in the Office Action of February 1, 2008. New claims 78 and 79 are added herein. Upon entry of this amendment, claims 56, 69, 78, and 79 will be pending in the application. The rejections are addressed individually below.

Claims 56 and 69 are amended herein to delete the limitation "that effects an alteration in late endosomal/lysosomal trafficking in the melanocyte, the alteration resulting in a decrease in melanin production in the melanocyte." Claim 56 is also amended to replace the term "production" with the term content. These amendments are supported by the specification, *inter alia*, at ¶¶ 133, 193, 241, and 344-346. Claims 56 is amended herein to limit the term "effective amount" to an effective amount of the one or more compounds being sufficient to reduce melanin content in the melanocyte. Claim 69 is amended herein to limit the term "pharmaceutically effective amount" to a pharmaceutically effective of the one or more compounds being sufficient to reduce skin pigmentation. These amendments are supported by the specification, for example at ¶¶ 31, 44, 217, and 229.

New claim 78 depends from claim 56, and adds the limitation wherein the melanocyte is in the skin of a mammal having a disease, disorder, or condition characterized by overproduction of melanin. New claim 79 depends from claim 69, and adds the limitation wherein the skin is the skin of a mammal having a disease, disorder, or condition characterized by overproduction of melanin. These amendments are supported by the specification, for example at ¶¶ 44 and 233.

The citations to the specification included throughout this response are to the paragraph numbers of the published application (US 2004/0175767).

I. Rejections Under 35 U.S.C. § 112, First Paragraph

A. Enablement

Claims 56 and 69 were rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly provides enablement for decreasing melanin *content* in a melanocyte, but not for decreasing melanin *production*. Claims 56 and 69 were also rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly fails to provide enablement for effecting an alteration in late endosomal/lysosomal trafficking (Office Action, pages 3-4).

Applicants' amended claim 56 recites "[a] method of decreasing melanin content in a melanocyte, the method comprising contacting the melanocyte with an effective amount of one or more compounds selected from the group consisting of" compounds of Formulae II-VIII. Amended claim 69 recites "[a] method of reducing skin pigmentation, the method comprising contacting skin of a mammal having a disease, disorder, or condition which is of a type that produces or overproduces melanin with a pharmaceutically effective amount of one or more compounds selected from the group consisting of" compounds of Formulae II-VIII.

As an initial matter, Applicants respectfully note that claim 69 does not recite the term "production." Therefore, Applicants traverse this rejection with respect to claim 69.

Without acquiescing in the propriety of the rejection of claim 56, and solely to expedite prosecution, Applicants have amended claim 56 to replace the term "production" with the term "content," and to delete the limitation "a compound that effects an alteration in late endosomal/lysosomal trafficking."

Accordingly, Applicants respectfully aver that this enablement rejection under § 112, first paragraph has been overcome, and respectfully request withdrawal of the same.

B. Written Description

Claims 56 and 69 were rejected under 35 U.S.C. § 112, first paragraph, as having "no written basis for the newly added plural limitation 'or more compounds' as recited in amended claims 56 and 69." Office Action, page 3. Applicants traverse this rejection.

Support for the limitation "one or more compounds" is found throughout the specification, for example, at ¶¶ 29, 215, 223-226, 235, and 237. Therefore, this limitation has written support in the specification and does not represent new matter.

Accordingly, Applicants respectfully request that this § 112, first paragraph, written description rejection be reconsidered and withdrawn.

II. Rejection Under 35 U.S.C. § 102(b)

Claims 56 and 69 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. 3,389,051 ("Kagan"). The Office Action asserts that Kagan inherently anticipates Applicants' claims. Applicants respectfully disagree.

Under 35 U.S.C. § 102(b), "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). *See also* MPEP § 2112 at 2100-47. "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original). *See also* MPEP § 2112 at 2100-48.

Claims 56 and 69 have been amended as described in Part I above.

Kagan discloses methods for reducing cholesterol in the body by administering particular chemical compounds, which include Applicants' compound VIII (col. 1, line 1 – col. 2, line 12; col.

2, lines 36-40). The disclosure of Kagan is focused on compositions for *oral* administration or *injection* for reducing cholesterol levels, and does not teach or suggest topical administration of the disclosed cholesterol-lowering compositions for any purpose (*see, e.g.*, col. 4, lines 69-75; col. 5, lines 61-66; Examples 1-8; claims 1-2).

Kagan does not expressly or inherently disclose each and every element of Applicants' claimed methods, because Kagan's disclosure is focused on systemic administration of drugs to lower cholesterol. There is no teaching in Kagan that oral administration of cholesterol-lowering drugs has any affect on melanogenesis or specifically that skin is lightened (from a decrease in melanin production in melanocytes) when these drugs are administered systemically. Kagan does not teach a method of contacting skin or melanocytes with a compound of Formulae II-VIII, and thus cannot anticipate Applicants' claims under § 102(b).

Kagan discloses a wide range of *oral* and *parenteral* formulations for administering the disclosed cholesterol lowering compounds (*see, e.g.,* col. 4, line 69 - col. 5, line 66; Examples 1-8). For example, at column 4, lines 70-75, Kagan states that "the novel compositions are suitably presented for administration in unit dosage form as tablets, pills, capsules, powders, wafers, cachets, granules, sterile parenteral solutions or suspensions in aqueous or oil vehicles, oral aqueous or oil dispersions, including syrups and elixirs, and the like." However, Kagan does *not* disclose administration to the skin as melanocytes, or identify compositions *formulated for topical* administration. Indeed, by disclosing numerous oral and parenteral dosage forms but failing to disclose topical formulations, the teachings of Kagan suggest to one of ordinary skill in the art that the disclosed compositions would not be effective for their intended purpose (lowering cholesterol) when administered to the skin or melanocyte. Kagan certainly does not teach that practicing its disclosed methods would necessarily result in contacting skin or melanocytes with the disclosed cholesterol-lowering compounds.

Additionally, the Office Action admits that "Kagan does not explicitly teach the specifically claimed compound of formula VIII and is silent with respect to decreasing melanin production in a melanocyte or reducing skin pigmentation." (Office Action, page 8). The Office Action also

admits that "Kagan does not expressly teach decreasing melanin production in a melanocyte (claim 56) or reducing skin pigmentation (claim 69) as a result of the administration of the disclosed compounds to either the subject or the cell cultures ...." (Office Action, page 9) (emphasis added). Therefore, Kagan does not expressly anticipate claims 56 and 69 under § 102(b).

Furthermore, the Office Action fails to establish that "the missing descriptive matter is necessarily present in the thing described in the reference" as required by *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999). The Office Action does not establish that the compounds disclosed in Kagan were ever topically administered to skin, or that systemic administration affects melanin production. The Office Action also fails to establish that a melanocyte was ever necessarily contacted with the compounds disclosed in Kagan.

Additionally, new claims 78-79 recite the limitation that the methods are used to treat a mammal having a disease, disorder, or condition characterized by overproduction of melanin. Kagan teaches a method of reducing *cholesterol* content, not *melanin* content. Thus Applicants' methods recited in claims 78-79 are also distinct from those disclosed by Kagan, and are not anticipated under § 102(b).

In sum, Kagan does not teach or suggest every element of Applicants' claims directed to administering compounds to skin or melanocytes to reduce melanin content or skin pigmentation in a mammal in need of such treatment. Accordingly, Applicants respectfully submit that claims 56 and 69, as currently amended, are not inherently anticipated under § 102(b).

Thus, it is requested that this § 102(b) rejection be reconsidered and withdrawn.

III. Conclusion

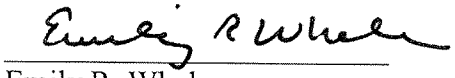
In view of the above amendment and arguments, Applicants believe the rejections in the Office Action of February 1, 2008 have been overcome and the pending claims are in condition for allowance.

If there are any questions, the Examiner is encouraged to call the undersigned to expedite prosecution.

Applicants believe no fee is due with this response. However, please charge any underpayments or credit any overpayments to our Deposit Account No. 08-0219, under Order No. 0291472.00124US2 from which the undersigned is authorized to draw.

Respectfully submitted,

Dated: 4/23/08



Emily R. Whelan
Registration No.: 50,391
Attorney for Applicant(s)

Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, Massachusetts 02109
(617) 526-6000 (telephone)
(617) 526-5000 (facsimile)